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(54) Title: INTEGRASE COFACTOR

(57) Abstract: In a study of HIV-1 integrase (IN) complexes derived from nuclei of human cells stably expressing the viral protein from a synthetic gene it was demonstrated that in the nuclear extracts IN exists as part of a large distinct complex with apparent Stokes radius of 61Å, which dissociates upon dilution yielding a core molecule of 41 Å. The IN complexes were isolated from cells expressing FLAG-tagged IN. By present invention it was demonstrated that the 41Å core is tetramer of IN, whereas 61 Å molecules are composed of IN tetramers associated with a cellular protein with an apparent molecular weight of 76 kDa. This integrase interacting protein (Inip76) was found to be identical to LEDGF/DFS70/p75 a protein implicated in regulation of gene expression and cellular stress-response. HIV-1 IN and Inip76 co-localized in the nuclei of human cells stably expressing IN. Furthermore, it has been demonstrated by present invention that recombinant Inip76 strongly promoted strand-transfer activity of HIV-1 IN in vitro. Our findings reveal that the minimal IN molecule in human cells is a tetramer and clearly demonstrates that Inip76 is plays a role in retroviral integration. Therefore the present invention provides integrase interacting proteins and more particularly cofactors which promote strand transfer activity of viral integrase, more particularly HIV integrase, and methods and uses relating thereto. The present invention relates to a cellular protein that associates with integrase (integrase interacting protein-Inip), to molecules interacting with Inip and their use as an antiviral. The present invention also relates to antibodies, RNA interference, antigen therapy, gene silencing or antisense inhibition of said integrase interacting protein. The novel integrase interaction protein is a target for HIV replication prevention or inhibition.

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